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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,847	03/30/2001	Peter J. Sims	26336-23	7002

23579 7590 10/31/2003

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,847	SIMS ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-33 and 59-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-33 and 59-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

The request filed on 7/25/03 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/823847 is acceptable and a RCE has been established. An action on the RCE follows.

In paper no. 23, applicant amended claims 26, 29, 30, 33, 59, 62, 63, 65, 66 and cancelled claims 34 and 67. Claims 26-33 and 59-66 are under consideration.

Sequence Compliance

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. A specific example within the specification that does not comply with the sequence rules is found Table 1 on page 56, which lists exon and intron sequences without a SEQ ID NO. Applicant is required to append a SEQ ID NO. to any sequence applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

Appropriate correction is required.

Double Patenting

Claims 59-66 objected to under 37 CFR 1.75 as being a substantial duplicate of claims 26-33. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 59-66 are drawn to a method of preventing viral infection by introducing a Phospholipid Scramblase polypeptide or fragment into a cell, while claims 26-33 are drawn to method of inhibiting viral infection by introducing a Phospholipid Scramblase polypeptide or fragment into cells. "Inhibiting" and "preventing" viral infection is not distinguishable, as each verb is drawn to prophylactic intervention. Also, claims 26-33 require introducing the instant polypeptide into cells to inhibit viral infection, while claims 59-66 are drawn to introducing the same polypeptide into a cell (emphasis added). The original claim set (26-33) encompasses introduction of the polypeptide into individual cells within a population. Therefore, the subject matter of claims 59-67 is indistinguishable from the subject matter of claims 26-33, respectively.

Applicant argues that the "inhibiting" refers to arresting the development of disease while "preventing" refers to stopping the initiation of disease.

In response, "arresting" and "stopping" disease are synonyms. These verbs mean the same thing. Therefore, it is maintained that claims 56-66 are substantial duplicates of claims 26-33.

Applicant further asserts that the skilled artisan would understand that various methodologies may be used to assess the development of a disease.

However, the two sets of claims are not drawn to different methodologies. They are both drawn to preventing, inhibiting, stopping and arresting viral infection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-33 and 59-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record.

Applicant states that the results in example 4 indicate that the phospholipid scramblase cooperates with other IFN-induced proteins to inhibit VSV replication. Applicant points out that expression of PLSCR1 results in a 26% increase in viable cells and argues that the results of example 4 clearly show inhibition of the disease state of the transfected cell line. Applicant admits, however, that the results of example 4 do not relate to preventing disease. Applicant asserts that the method of inhibiting viral infection by introducing Phospholipid Scramblase to prevent virus budding has been reduced to practice.

Applicant's arguments have been fully considered, but are found unpersuasive. It is maintained that the results of example 4 are ambiguous as to whether the cytokine or the enzyme had a direct effect on VSV replication. The increase in viable cells does not provide adequate evidence for "inhibiting viral infection", which is required by the claims. There is only a slight reduction of viral yield with the enzyme alone. Further, in view of the synergism between IFN-β and Hu-PLSCR1, discussed by applicant, it is maintained that the data presented in example 4 is ambiguous. Contrary to applicant's assertion, the instant method of inhibiting viral infection by introducing Phospholipid Scramblase has not been reduced to practice.

There are also a number of other issues have not been addressed by applicant. These issues are reiterated here for the applicant's convenience. The scope of the instant method for

preventing viral infection is not limited to virus type, mode of transmission, infectivity or pathology. The claims encompass preventing viral infection in known viruses such as Ebola, Marburg, and HIV, with no art-recognized animal model. See the reviews of Wilson et al. (Cellular and Molecular Life Sciences. 2001; 58 (12-13): 1826-41) and Klein et al. (Clinical Therapeutics. 2000; 22 (3): 295-314) for general teaching in the art for HIV and Ebola vaccines. The specification does not teach an appropriate animal model for these viruses or use an animal model for other viruses to be inhibited.

In addition, the function of Phospholipid Scramblase is admittedly speculative; see the first paragraph on page 3 page 12, paragraph 50, and page 63, paragraph 177 of the specification. Further, on page 63, paragraph 177, the disclosure states that the presumed activity of phospholipid scramblase on cell membranes cannot be predicted by level of enzyme expression, but that other factors are involved. However, there is no teaching or indication that would enable one skilled in the art consider what these other unknown factors alluded to are.

The skilled artisan would also be unable to predict the effect of the enzyme merely by accomplishing its expression in a recombinant cell in vitro because the disclosure fails to teach effective delivery of Phospholipid Scramblase containing the PPxY motif in effective amounts to inhibit viral infection. The skilled artisan would be concerned about delivering such an enzyme or fragments thereof to cells because Phospholipid Scramblase function has not been clearly defined, see Sims et al. (Thrombosis and Haemostasis. 2001; 86 (1): 266-275, abstract only). There is also no teaching in the specification that addresses concerns in the art for effective delivery while not interrupting normal cellular function. There is no way to determine how the instant enzyme, delivered in such large quantities in order to bind every protein comprising a

WW motif would effect the host. This concern is also admitted in the specification at the top of page 64.

The claims also encompass delivering fragments that have the PPxY motif. It is maintained that the skilled artisan would be unable to make the scope of the claimed genus because the species are unrecognizable in view of the fact that the structural motif does not correlate with a recognized function. Therefore, the skilled artisan would be unable to determine whether a fragment containing the motif would have the required function because the function is not clearly defined by the inventors or the art, see page 3 page 12, paragraph 50, and page 63, paragraph 177 of the specification and the teachings of Sims et al. *supra*.

Applicant questions whether the rejection concerns a lack of enablement or written description. In response, enablement is concerned with whether "one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention" (emphasis added). In the instant case, the specification does not enable the skilled artisan a way to use the claimed invention for reasons discussed above nor does it provide a means for the skilled artisan to make the fragments containing the PPxY motif with the required function because the inherent function of the parent has not been defined.

Applicant asserts that the specification is replete with examples of peptides comprising PPxY, which inhibits viral budding and that the skilled artisan would be able to make peptides having the activity.

In response, while it is within the skill of the artisan to make PPxY motifs in peptides, it is beyond the skill of the artisan to confirm the functionality of the peptide fragments because the function of the parent is ambiguous. There is no clear example of viral inhibition in the

disclosure with the full parental sequence or with any peptide fragment containing the PPxY motif.

For these reasons, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make and/or use the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley